

Amendments to the Claim:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1 (original). A process for production of recombinant arylsulphatase A in a continuous cell culture system, the process comprising:

- i) culturing a mammalian cell capable of producing arylsulfatase A in liquid medium in a system comprising one or more bio-reactors;
- ii) concentrating, purifying and formulating the rhASA by a purification process comprising one or more steps of affinity chromatography and/or ion exchange chromatography

wherein the concentration and purification process of (ii) comprises a polishing step including a passive step, wherein the arylsulfatase A passes through a cation chromatography resin or membrane, and an active step, wherein the arylsulfatase A is detained within and subsequently eluted from an anion exchange membrane or resin, and wherein the cation chromatography resin or membrane and the anion chromatography membrane or resin are coupled or connected in a series.

2 (original). A process according to claim 1, wherein said mammalian cell comprises a nucleic acid sequence, which encodes:

- (a) the amino acid sequence of SEQ ID NO:2;
- (b) a portion of the sequence in (a), which is enzymatically equivalent to recombinant human arylsulfatase A
- (c) an amino acid sequence analogue having at least 75% sequence identity to any one of the sequences in (a) or (b) and at the same time comprising an amino acid sequence, which is enzymatically equivalent to recombinant human arylsulfatase A.

3-6 (cancelled).

7 (previously presented). A process according to claim 1, wherein the arylsulfatase A produced is selected from the group consisting of

- (a) the amino acid sequence of SEQ ID NO:3;
- (b) a portion of the sequence in (a), which is enzymatically equivalent to recombinant human arylsulfatase A
- (c) an amino acid sequence analogue having at least 75% sequence identity to any one of the sequences in (a) or (b) and at the same time being enzymatically equivalent to recombinant human arylsulfatase A.

8 (previously presented). A process according to claim 1, wherein the mammalian cells are of human or primate origin.

9 (previously presented). A process according to claim 1, wherein the concentration and purification process of ii) comprises one or more steps of Expanded Bed Chromatography.

10 (cancelled).

11 (previously presented). A process according to claim 1, wherein the concentration and purification process of ii) comprises the following steps:

- II) contacting an arylsulfatase A containing supernatant on an equilibrated chromatography column and eluting one or more fraction(s) containing arylsulfatase A;
- III) loading the fraction(s) from step II on another equilibrated chromatography column and eluting one or more fraction(s) containing arylsulfatase A;
- IV) buffer exchange of the arylsulfatase A present in the fraction(s) from step III by tangential flow filtration;
- V) polishing the preparation of arylsulfatase A from step IV in one or two or more successive steps, each step comprising loading the preparation on an equilibrated chromatography columns and eluting one or more fraction(s) containing arylsulfatase A;

- VI) passing the fraction(s) from step V through a viral reduction filter;
- VII) formulating the fraction(s) from step VI in order to obtain a preparation of arylsulfatase A in a suitable formulation buffer;
- VIII) optionally filling the formulated preparation of arylsulfatase A into a suitable container and freeze-drying the sample.

12 (original). A process according to claim 11, further comprising an initial step I) of concentrating the arylsulfatase A by tangential flow filtration.

13 (previously presented). A process according to claim 11, wherein the chromatography column used in step II of the purification process is an anion exchange column.

14 (original). A process according to claim 13, wherein said anion exchange column is a DEAE Sepharose column or a DEAE Streamline column.

15 (previously presented). A process according to claim 11, wherein the chromatography column used in step III of the purification process is a hydrophobic interaction column.

16 (previously presented). A process according to claim 11, wherein purification of the sample in step IV of the purification process is accomplished by tangential flow filtration.

17 (cancelled).

18 (previously presented). A process according to claim 11, wherein the filtration of the sample as performed in step VI of the purification process is replaced by or combined with contacting the sample with a detergent, preferably prior to step V or preferably prior to step Ii of the purification process.

19-23 (cancelled).

24 (previously presented). A formulation of aryl sulfatase A which is obtainable by a process according to claim 1, adapted for use as a medicament for reducing the sphingolipid 3-O-sulfogalactosylceramide levels within cells in the

peripheral nervous system and/or within the central nervous system in a subject suffering from and/or being diagnosed with metachromatic leukodystrophy.

25-31 (cancelled).

32 (previously presented). A method of treating/alleviating a symptom of a disorder associated with increased lysosomal storage of sphingolipid 3-O-sulfogalactosylceramide, said method comprising administering to a subject a formulation of arylsulfatase A obtained or obtainable by a process according to claim 1 and thereby obtaining a reduction in the galactosyl sulphatide levels in cells within the central nervous system of said subject.

33 (cancelled).

34 (previously presented). A method according to claim 36, said method comprising administering said formulation of arylsulfatase A by a route other than intracerebroventricular, spinal, intrathecal or intracranial administration.

35 (cancelled).

36 (previously presented). A method of treating/alleviating a symptom of a disorder associated with increased lysosomal storage of sphingolipid 3-O-sulfogalactosylceramide, said method comprising administering to a subject a pharmaceutical composition comprising recombinant arylsulfatase A and thereby obtaining a reduction in the galactosyl sulphatide levels in cells within the central nervous system of said subject.

37 (previously presented). A method according to claim 34, wherein said pharmaceutical composition is to be administered by intravenous or subcutaneous administration.

38 (previously presented). A method according to claim 37, wherein said pharmaceutical composition is to be administered on a daily, weekly, bi-weekly or monthly basis.

39 (previously presented). A method according to claim 32, wherein the formulation of arylsulphatase A comprises at least 98% bioactive aryl sulfatase A as determined by reverse phase

HPLC.

40 (previously presented). A method according to claim 32, wherein, said aryl sulfatase A has a specific activity of at least 20 U/mg.

41 (previously presented). A method according to claim 32, wherein said formulation does not comprise

- a) a vehicle for delivery of aryl sulfatase A into the central nervous system, and
- b) a component capable of causing opening or disruption of the blood brain barrier, and
- c) an intact cell.